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EUPHORBIA

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Euphorbia pilulifera, Linné (Nat. Ord. *Euphorbiaceæ*), is an annual, herbaceous plant, which occurs in nearly all tropical countries. It attracted considerable attention some years ago on account of its reputed value in the treatment of asthma, bronchitis, and other diseases of the respiratory organs, although it appears to have long been employed in India as a popular remedy for a great variety of other affections (compare 'Pharmacographia Indica,' Vol. III., p. 247).

According to Mr. J. H. Maiden,[1] Director of the Botanic Gardens, Sydney, N.S.W., the usefulness of the plant in pulmonary complaints was first brought to notice by Dr. Carr-Boyd, of Townsville, Queensland, about the year 1880, and it has therefore acquired in Australia the appellation of "Queensland Asthma Herb." The same author also notes that the herb from Fiji is said to be of better quality than that from Queensland, but inasmuch as it is a common weed in many countries, and, moreover, easily cultivated, any demand for it could readily be supplied.

The observations regarding the remedial value of the plant are by no means concordant, for although regarded by some as possessing no action of a definite and distinctive nature, the experience of others has indicated that it is capable of affording relief in many cases of asthma, but on no account to be considered a specific in this disease.

The chemical examinations which have heretofore been made of this species of *Euphorbia* appear to have only shown the presence of such common constituents of plants as resin, wax, tannin, sugar, mucilage, etc., and not to have resulted in the isolation of any definite compound. So far as known to us, the most recently published communication on the subject was by Mr. J. Stableford Hill,[2] who, however, recorded only

* Communication from the Wellcome Chemical Research Laboratories, London, E.C., to the Pharmaceutical Society of Great Britain, April 8, 1913, and reprinted from *The Pharmaceutical Journal and Pharmacist*, April 12, 1913.

1 *Pharmaceutical Journal*, 1893, **63**, 166.

2 'Year-Book of Pharmacy,' 1909, p. 325.

the results of a preliminary examination, and his investigation appears not to have been further pursued. It was noted by Mr. Hill (*loc. cit.*) that indications were obtained of the presence of a small amount of alkaloid, but the isolation of such a constituent was not effected.

In view of the attention which the plant in question has received with respect to its medicinal properties, it was deemed desirable to subject it to a complete chemical examination. The results of the present research are summarised at the end of this paper.

Experimental.

The material employed for this investigation was obtained directly from the Fiji Islands, through the kindness of Captain F. L. Langdale, of Wakaya, Fiji, and consisted of the entire, freshly collected, and air-dried plant.

A small portion (10 grammes) of the ground material was extracted with Prollius' fluid, and the resulting liquid examined in the usual manner for the presence of an alkaloid, but the reactions obtained were very slight.

Another portion (20 grammes) of the material was successively extracted in a Soxhlet apparatus with various solvents, and the resulting extracts dried in a water-oven until of constant weight.

Petroleum (b.p. 35-50°) extracted	0·37	gramme	= 1·85	per cent.
Ether ..... ,,	0·32	,,	= 1·60	,,
Chloroform ..... ,,	0·16	,,	= 0·80	,,
Ethyl Acetate ..... ,,	0·80	,,	= 4·00	,,
Alcohol.. ..... ,,	1·30	,,	= 6·50	,,
Total	2·95	grammes	= 14·75	per cent.

For the purpose of a complete examination of the plant, 20·07 kilogrammes of the ground material were extracted by continuous percolation with hot alcohol. After the removal of the greater portion of the alcohol, there remained a viscid, dark green extract, amounting to 3·94 kilogrammes.

Distillation of the Extract with Steam.—Separation of an Essential Oil.

The entire amount of the above-mentioned alcoholic extract was mixed with water and distilled in a current of steam On extracting the distillate with ether, and removing the solvent, a small amount (3·7 grammes) of an essential oil was obtained. This was redistilled, when it passed over almost entirely between 235° and 260° as a pale yellow liquid, which gave the colour reaction of furfuraldehyde.

Non-Volatile Constituents of the Extract.

After the above-described operation there remained in the distillation vessel a dark brown, aqueous liquid (A), together

with a quantity of a dark green, soft resin (B). The latter was separated, and thoroughly washed with hot water, the washings being added to the main portion of the aqueous liquid.

Examination of the Aqueous Liquid (A).

The aqueous liquid was concentrated under diminished pressure, and then repeatedly extracted with ether. These ethereal liquids were united, concentrated somewhat, and then extracted with 2 per cent. hydrochloric acid, after which the ethereal liquid was washed with water. The combined aqueous acid liquid and washings contained nothing alkaloidal, but deposited a small amount of a yellow, indistinctly crystalline substance. This was collected and treated with boiling alcohol, in which it appeared to be almost insoluble. It dissolved, however, in hot pyridine, from which it separated in small, needle-shaped crystals, which contained solvent of crystallisation and did not melt at 335°. The amount of this substance was only 0·04 gramme, but a larger quantity was subsequently obtained from the chloroform extract of the resin, when it was identified as jambulol, $C_{16}H_3O_4(OH)_5$.

Isolation of Gallic Acid.

The combined acid liquid and aqueous washings, from which the above-described substance had separated, were extracted many times with ether, when a semi-crystalline product was obtained. This was treated with hot chloroform, which removed some colouring matter, after which it was crystallised from ethyl acetate. A substance was thus obtained in small, nearly colourless needles, which melted and decomposed at 250-253°.

0·0809* gave 0·1460 CO_2 and 0·0289 H_2O. C=49·2; H=4·0.
$C_7H_6O_5$ requires C=49·4; H=3·5 per cent.

This substance was thus found to be gallic acid, with which it agreed in all its properties. Its identity was further confirmed by the preparation of the trimethyl derivative, which separated from ethyl acetate in flat needles, melting at 164-165°.

After shaking the ethereal extract with dilute hydrochloric acid, as above described, it was extracted successively with aqueous ammonium carbonate, sodium carbonate, and sodium hydroxide. On finally evaporating the ether, only a trace of oily material remained. Each of the alkaline liquids was acidified, when from the sodium carbonate extract a considerable amount of a yellow substance separated, which was collected. The acidified ammonium carbonate and sodium hydroxide extracts were extracted with ether, when the former yielded a further small amount of gallic acid, and the latter only a trace of amorphous material.

* Dried at 120°.

Isolation of Quercetin, $C_{15}H_{10}O_7$.

The substance which had separated from the above-mentioned sodium carbonate extract on acidification was crystallised several times from dilute alcohol. It was thus obtained in microscopic, yellow needles, which melted and decomposed at 308-310°, and amounted to 1·7 gramme.

0·0792* gave 0·1718 CO_2 and 0·0257 H_2O. C = 59·2; H = 3·6.
$C_{15}H_{10}O_7$ requires C = 59·6; H = 3·3 per cent.

The composition and characters of this substance clearly indicated it to be quercetin. Its identity was confirmed by the preparation of the acetyl derivative, which was obtained in small, colourless needles, melting at 194-195°.

The aqueous liquid (A), which had been completely extracted with ether, was shaken with twenty successive portions of warm amyl alcohol. The united amyl-alcoholic liquids, after being somewhat concentrated under diminished pressure, were washed with water until free from sugar. The amyl alcohol was then removed so far as possible under diminished pressure, and finally by distillation in a current of steam. After removal of the water under diminished pressure, and subsequent drying at 100°, there remained 180 grammes of a dark, syrupy product. This was heated with 5 per cent. sulphuric acid in a reflux apparatus for about three hours, and the mixture then distilled in a current of steam. On extracting the distillate with ether, and removing the solvent, a small amount of an oily liquid was obtained which gave the colour reaction of furfuraldehyde. The acid liquid remaining in the distillation flask was then repeatedly extracted with ether, and the ethereal liquids united and concentrated, when a small amount of a yellow substance separated, which was collected. On subsequently shaking the ethereal liquid with aqueous ammonium carbonate a little gallic acid was removed, whereas the products obtained by extraction with aqueous sodium carbonate and sodium hydroxide, as well as by the final evaporation of the ether, yielded nothing definite. After having extracted the aqueous, acid liquid with ether, as above described, it was divided into two equal portions. From one portion the sulphuric acid was removed by treatment with baryta and subsequent precipitation of the excess of the latter by carbon dioxide. After concentrating the filtered liquid it was found to contain a considerable quantity of sugar, since it readily yielded *d*-phenylglucosazone (m.p. 214-217°), and the presence of some glucosidic material in the amyl alcohol extract was thus indicated. To the other portion of the aqueous, acid liquid such an amount of potassium hydroxide was added as to represent 10 per cent. of its weight of free alkali. The alkaline liquid was first heated for a few minutes to boiling, then poured into an excess of cold dilute acid, and the mixture extracted many times with ether. These ethereal

* Dried at 120°.

liquids were united and concentrated, when a small amount of yellow substance was deposited, similar to that obtained by the above-described acid hydrolysis. The filtered ethereal liquid was subsequently extracted with aqueous alkalis, but nothing further than a trace of gallic acid was thus obtained.

Isolation of a New Phenolic Substance, $C_{28}H_{18}O_{15}$.

The yellow substance which had been deposited from the above-mentioned ethereal liquids was insoluble in a solution of ammonium carbonate, but dissolved in aqueous sodium carbonate, and was reprecipitated on acidification. It was apparently insoluble in chloroform, benzene, and the higher boiling fractions of petroleum, but soluble in warm water, alcohol, and glacial acetic acid, and readily soluble in pyridine. It contained no nitrogen. Considerable difficulty was experienced in purifying the substance, but after several crystallisations from dilute alcohol a small quantity (0·15 gramme) was finally obtained which appeared perfectly homogeneous and formed microscopic clusters of needles. It did not melt, but appeared to decompose, at about 340°. The substance was found to separate with varying amounts of water of crystallisation, and for the purpose of analysis it was dried at 130°.

0·0549 gave 0·1134 CO_2 and 0·0154 H_2O. C = 56·3; H = 3·1.
0·0618 ,, 0·1280 CO_2 ,, 0·0175 H_2O. C = 56·5; H = 3·1.
$C_{28}H_{18}O_{15}$ requires C = 56·6; H = 3·0 per cent.

The above-described substance was evidently phenolic, and an attempt was therefore made to obtain both an acetyl derivative and a methyl ether, but from the small amount of material available no crystalline product could be obtained.

After the extraction of the aqueous liquid (A) by amyl alcohol, the last traces of this solvent were removed in a current of steam, and the aqueous liquid then kept for some time, when a considerable quantity (about 40 grammes) of dark brown, amorphous material was deposited. As nothing could be directly isolated from this material, it was heated with 5 per cent. sulphuric acid, and the mixture then distilled in a current of steam, when a very small amount of a volatile, oily liquid was obtained, which gave the colour reaction of furfuraldehyde. The aqueous, acid liquid remaining in the distillation flask was extracted many times with ether, and afterwards treated with baryta for the removal of the sulphuric acid, but on subsequent concentration no definite osazone could be prepared from it. The ethereal liquids were united and concentrated, when a small amount of yellow substance was deposited. After the separation of the yellow substance by filtration, the ethereal liquid was shaken with aqueous ammonium carbonate, which removed practically all of the dissolved material, but from which only a trace of

gallic acid could be isolated. The sparingly soluble yellow substance was similar in all its properties to the above-described compound, $C_{28}H_{18}O_{15}$, and its analysis indicated it to consist of the latter in a slightly impure state. (Found, C=57·6; H=3·1. Calc., C = 56·6; H = 3·0 per cent.)

The aqueous liquid (A) from which the above-mentioned brown, amorphous material had been removed, was next treated with a slight excess of a solution of basis lead acetate, when an abundant precipitate was produced, which was collected and thoroughly washed with water. A portion of this precipitate was suspended in water, decomposed by hydrogen sulphide, and the mixture filtered. The clear liquid gave a dark colouration with ferric chloride, but no precipitate with gelatin, and it therefore appeared to contain no tannin. Nothing definite could be isolated from this liquid, either directly or after heating with a 10 per cent. solution of potassium hydroxide.

The filtrate from the basic lead acetate precipitate was deprived of lead by means of hydrogen sulphide, again filtered, and the resulting liquid concentrated under diminished pressure to the consistency of a thin syrup. The latter evidently contained a considerable proportion of sugar, since it readily yielded *d*-phenylglucosazone (m.p. 218-220°). A portion of the concentrated syrup was acetylated, but no crystalline derivative of the sugar could be obtained, and on hydrolysing the acetylated product with dilute sulphuric acid it yielded a sugar which was strongly lævorotatory, thus indicating the latter to have consisted, at least chiefly, of lævulose. Another portion of the original syrupy liquid was heated for some time with 5 per cent. sulphuric acid, and the mixture distilled in a current of steam. A small amount of a yellowish oil was thus obtained, which gave the furfuraldehyde colour reaction. On heating a portion of the syrup with an alkali hydroxide it evolved ammonia, but a solution of mercuric nitrate gave only a slight brownish precipitate, from which no trace of a crystalline compound could be obtained.

The entire remaining portion of the syrupy aqueous liquid was finally made alkaline, and extracted successively with ether, chloroform, and warm amyl alcohol. All these solvents removed traces of amorphous material, which, when dissolved in a little dilute acid, gave slight alkaloid reactions. These results thus confirmed the reactions obtained in the preliminary test for an alkaloid by extracting the herb with Prollius' fluid, but the amount of basic substance present was evidently very small and of an indefinite character.

Examination of the Resin (B).

The soft, resinous material, which had been separated from the aqueous liquid as previously described, was dissolved in hot alcohol, mixed with purified sawdust, and the thoroughly dried mixture extracted successively in a large Soxhlet apparatus with various solvents. The amounts of the different

extracts thus obtained, when dried in a water-oven, were as follows :—

Petroleum (b.p. 35-50°)	extracted	378	grammes
Ether	,,	40	,,
Chloroform	,,	142	,,
Ethyl Acetate	,,	20	,,
Alcohol	,,	65	,,
Total		645	grammes

As the above amount of resin was obtained from 20·07 kilogrammes of the air-dried plant, it represented about 3·2 per cent. of its weight.

Petroleum Extract of the Resin.

This extract, before the removal of the solvent, deposited about 9 grammes of sparingly soluble material, which was collected, and extracted successively in a Soxhlet apparatus with ethyl acetate and alcohol. The latter solvent removed practically nothing, but from the ethyl acetate extract there separated a quantity of crystalline substance, which had a green colour, due to chlorophyll. The crystalline substance was found to be identical with an alcohol, $C_{25}H_{40}O$, which was subsequently obtained in larger amount from the petroleum extract after its hydrolysis, and is fully described below. After the separation of the above-mentioned material from the petroleum extract by filtration, the solvent was removed and the residue treated with ether, when a small amount of substance remained undissolved.

Isolation of Melissic Acid, $C_{30}H_{60}O_2$, and Triacontane, $C_{30}H_{62}$.

The above-mentioned substance, sparingly soluble in ether, was completely dissolved by ethyl acetate, from which it separated in an amorphous form. To effect its purification it was first distilled under diminished pressure, after which it was treated with an alcoholic solution of potassium hydroxide. An acidic portion was thus removed, which was again distilled under diminished pressure, and subsequently crystallised from ethyl acetate, when it melted constantly at 89-90°, and amounted to 0·04 gramme.

0·0767* gave 0·2239 CO_2 and 0·0915 H_2O. C = 79·6 ; H = 13·3.
$C_{30}H_{60}O_2$ requires C = 79·7 ; H = 13·3 per cent.

This substance was evidently melissic acid, and its identity was further confirmed by the preparation of its methyl ester melting at 73-74°.

The material which had been separated from the melissic acid was heated to 135° with an equal weight of phthalic anhydride for about two hours. The product was then dissolved in a mixture of chloroform and ether, and shaken with aqueous sodium carbonate, when a small amount of a solid

* Dried at 110°.

separated, which was evidently the sodium salt of an acid phthalic ester. This was hydrolysed, and a trace of a fatty alcohol thus obtained, which, after crystallisation, melted at 77-78°, and probably consisted of ceryl alcohol. The chloroform-ether liquid was subsequently evaporated, and the residue heated with an alcoholic solution of potassium hydroxide in order to eliminate any unchanged phthalic anhydride, after which the alkaline product was extracted with ether. A small amount of a hydrocarbon was thus obtained, which, after crystallisation from a mixture of ethyl acetate and alcohol, melted at 65-66°.

0·0642* gave 0·2005 CO_2 and 0 0824 H_2O. C = 85·2; H = 14·3.
$C_{30}H_{62}$ requires C = 85·3; H = 14 7 per cent.

This substance was thus shown to be a hydrocarbon, and its melting point indicated it to be triacontane.

The ethereal solution of the petroleum extract, from which the above-described substances had been separated, was next shaken with a 20 per cent. aqueous solution of potassium hydroxide and afterwards washed with water. By this treatment emulsions were formed, which separated with difficulty, and only a small amount of fatty material was thus removed. The solvent was accordingly evaporated from the ethereal liquid, and the residue heated with an alcoholic solution of potassium hydroxide, after which water was added, the alcohol removed, and the alkaline, aqueous mixture extracted with ether. On evaporating this ethereal liquid a quantity of unsaponifiable material was obtained, which was fractionally crystallised from a large volume of alcohol. The first three fractions contained a substance which, when dissolved in chloroform with a little acetic anhydride, gave on the addition of sulphuric acid a pink colouration. The fourth and fifth fractions consisted of material melting below 100°, whilst the residual portion formed a thick syrup, which could not be distilled under diminished pressure, and from which no fatty alcohol could be obtained by treatment with phthalic anhydride. The combined fourth and fifth fractions were treated with phthalic anhydride in the manner already described, when an alcohol was obtained which, after crystallisation from a mixture of ethyl acetate and alcohol, melted constantly at 77·5-78·5°. It was dried at 120° and analysed.

0·0792 gave 0·2398 CO_2 and 0·0984 H_2O. C = 82·6; H = 13·8.
0·0617 gave 0·1866 CO_2 and 0·0784 H_2O. C = 82·5; H = 14·1.
$C_{27}H_{56}O$ requires C = 81·8; H = 14·1 per cent.

The characters and composition of this substance thus indicated it to consist of slightly impure ceryl alcohol.

The portion of material which did not combine with the phthalic anhydride by the above treatment appeared to consist of a mixture of a hydrocarbon and a phytosterol, which

* Dried at 110°.

were first separated as completely as possible by fractional crystallisation. About 0·2 gramme of a hydrocarbon was thus obtained, which melted constantly at 62-63°, and evidently was a further small amount of the previously identified triacontane, $C_{30}H_{62}$ (Found, C = 84·8; H = 14·5. Calc., C = 85·3; H = 14·7 per cent.). The phytosterol fraction was acetylated, and, after several crystallisations of the product, 0·08 gramme of a substance was obtained which melted at 122-123°. On hydrolysing the latter it yielded a compound which crystallised in flat needles, melting at 132-133°, and which gave the colour reaction of the phytosterols, but the amount was not sufficient for analysis.

Isolation of a New Monohydric Alcohol, Euphosterol, $C_{25}H_{39}\cdot OH$.

The above-mentioned, first three fractions of unsaponifiable material, after repeated crystallisation from high-boiling petroleum, yielded a substance which separated in long, colourless needles, melting at 268°. By similar treatment of the material deposited by the original petroleum extract, as above noted, a further small amount of the same substance was obtained. The substances were united, acetylated, and the product fractionally crystallised from high-boiling petroleum, when about 0·6 gramme of colourless needles was finally obtained, which melted constantly at 295-297°. A portion of this acetyl derivative was hydrolysed, when it yielded an alcohol which separated from high-boiling petroleum in needles melting at 274-275°. After drying at 120° it was analysed.

0·0710 gave 0·2190 CO_2 and 0·0735 H_2O. C = 84·1; H = 11·5.
0·0762 ,, 0·2349 CO_2 ,, 0·0790 H_2O. C = 84·1; H = 11·5.
$C_{25}H_{40}O$ requires C = 84·3; H = 11·2 per cent.

From these results the above-described compound may be considered to possess the formula $C_{25}H_{40}O$, in which case it would be isomeric with homotaraxasterol,[3] but the possibility is not excluded of its being the next lower homologue of the latter, namely, $C_{24}H_{38}O$, which requires C = 84·2; H = 11·1 per cent. It is, however, a new compound, and, with reference to its characters and source, has been designated *euphosterol.*

When euphosterol is dissolved in chloroform with a little acetic anhydride, and a few drops of concentrated sulphuric acid subsequently added, a pink colour is produced, which slowly darkens. This colour reaction is very similar to that given by some other monohydric alcohols previously isolated in these laboratories, namely, androsterol, $C_{30}H_{50}O$, and homoandrosterol, $C_{27}H_{44}O$,[4] taraxasterol, $C_{29}H_{48}O$, and homotaraxasterol, $C_{25}H_{40}O$ (*loc. cit.*). It is to be presumed that these compounds are all members of an homologous series, which is represented by the general formula, $C_nH_{2n-10}O$. Euphosterol differs, however, appreciably from the other

[3] *Journ. Chem. Soc.*, 1912, **101**, 2,425.
[4] *Ibid.*, 1909, **95**, 739.

known members of tho series by its higher melting-point, and by being apparently devoid of optical activity, but, as its acetyl derivative showed a slight rotation, this apparent inactivity was probably due to its very sparing solubility, which also precluded a determination of its molecular weight.

Acetyleuphosterol, $C_{25}H_{39}O{\cdot}CO{\cdot}CH_3$. — This compound (m.p. 295-297°), tho preparation of which has already been described, was dried at 125° and analysed.

0·0730 gave 0·2172 CO_2 and 0·0716 H_2O. C = 81·1; H = 10·9.
0·0645 ,, 0·1924 CO_2 ,, 0·0640 H_2O. C = 81·3; H = 11·0.
$C_{27}H_{42}O$ requires C = 81·4; H = 10·6 per cent.

A determination of its optical activity gave the following result :—

0·3239, made up to 20 C.c. with chloroform, gave α_D + 0·16′ in a 2-dcm. tube, whence $[\alpha]_D$ + 8·2°

Bromoacetyleuphosterol.—A small amount (0·1 gramme) of acetyleuphosterol was brominated in the cold in chloroform solution, and the product crystallised from a mixture of ethyl acetate and alcohol, when it separated in small needles, melting at 183-186°.

In the course of separating the above-described acetyleuphosterol from the original acetylated product by fractional crystallisation, several indefinite fractions of lower melting point were obtained. Two of these, dried at 120°, were analysed.

M.p. 205–210°. 0·1023 gave 0·3077 CO_2 and 0·1050 H_2O.
C = 82·0; H = 11·4 per cent.
M.p. 230–260°. 0·0895 gave 0·2769 CO_2 and 0·0933 H_2O.
C = 84·4; H = 11 6 per cent.

It thus appears probable that euphosterol was accompanied in the original acetylated product by some other alcohols of the same series.

The alkaline, aqueous mixture resulting from the hydrolysis of the petroleum extract, and which had been extracted with ether for the removal of unsaponifiable material, as above described, was next acidified and again extracted with ether. During this operation an emulsion was formed, which was separated and washed with ether, theso washings being added to the main portion of the ethereal liquid. After this treatment there was obtained from the emulsion a small amount of solid material, which was mixed with purified sawdust and extracted successively in a Soxhlet apparatus with ethyl acetate and absolute alcohol. The ethyl acetate removed a small amount of substance, from which about 0·35 gramme of melissic acid was obtained. (Found, C = 79·7; H = 13·3. Calc., C = 79·7: H = 13·3 per cent.).

Isolation of a Phytosterolin (Phytosterol Glucoside).

After extracting the above-mentioned material with ethyl acetate, it yielded to absolute alcohol a small amount sub-

stance, which, when dissolved in acetic anhydride and chloroform, and a few drops of concentrated sulphuric acid added, gave the colour reaction of the phytosterols. In order to effect its purification it was acetylated, and the product so obtained crystallised several times, when it separated in flat needles, melting at 161-162°. This acetyl derivative was then hydrolysed, and the resulting compound crystallised from dilute pyridine. It was thus obtained in small, colourless needles, which melted and decomposed at 297°. After drying at 130°, it was analysed.

0·0631 gave 0·1651 CO_2 and 0·0595 H_2O. C = 71·4 ; H = 10·5.

A glucoside of sitosterol or i s isomerides, $C_{33}H_{56}O_6$, requires C = 72·3 ; H = 10·2 per cent., and although the composition of the above-described compound is not in complete agreement with these figures, its characters permit of no doubt that it belongs to the class of phytosterolins (compare *Journ. Chem. Soc.*, 1913, **103**, 399). A further quantity of an apparently identical substance was obtained from the ether extract of the resin, but the total amount available was not sufficient for subjecting it to acid hydrolysis.

Examination of the Fatty Acids.

As mentioned above, the aqueous, alkaline liquid from which the unsaponifiable material has been removed was acidified and extracted with ether. The ethereal solution of the fatty acids was dried and the solvent evaporated, after which the product was esterified by treatment with methyl alcohol and sulphuric acid. The resulting esters were distilled three times under diminished pressure, and the following fractions collected: 185-197°, 197-200°, 200-218°, 218-240°/10 Mm. These fractions were separately hydrolysed, and yielded in all 88 grammes of fatty acid. The first two fractions melted at 61-62° and 62-63° respectively. They were therefore united, crystallised from alcohol, and analysed (Found, C = 74·4 ; H = 12·2. $C_{16}H_{32}O_2$ requires C = 75·0 ; H = 12·5 per cent). It thus appeared probable that the first two fractions consisted of palmitic acid with a small proportion of an acid of lower carbon content.

The third and fourth fractions of acid were united, and then by means of their lead salts separated into solid and liquid portions, which were further examined.

The Solid Acids.—These acids, after two crystallisations from alcohol, melted at 55°. As they evidently consisted of a mixture, they were united with the above-mentioned, first two fractions of solid acid, and the whole esterified by means of methyl alcohol and sulphuric acid. The product was then distilled under diminished pressure, and the distillate collected in three fractions, which had the following characters and composition:

I. B.p. below 183°/10 Mm. M.p. 24°.
0·1027 gave 0·2772 CO_2 and 0·1115 H_2O. C = 73·6; H = 12·1.
II. B.p. 183-185°/10 Mm. M.p. 26-27°.
0·1084 gave 0·3005 CO_2 and 0·1241 H_2O. C = 75·6; H = 12·7.
III. B.p. 185-205°/10 Mm. M.p. 24-25°.
0·0850 gave 0·2364 CO_2 and 0·0968 H_2O. C = 75·8; H = 12·6.
Methyl palmitate, $C_{17}H_{34}O_2$, requires C = 75·6; H = 12·6 per cent.

These results indicate that the second fraction consisted of practically pure methyl palmitate, whilst the first and third fractions appear to contain, in addition to the latter, small amounts of acids (in the form of esters) of lower and higher carbon content respectively.

The Liquid Acids.—These acids distilled between 223 and 235°/10 Mm., and amounted to about 19 grammes. An analysis and a determination of the iodine value gave the following results:—

0·0947 gave 0·2664 CO_2 and 0·0958 H_2O. C = 76·7; H = 11·2.
0·2393 absorbed 0·3436 Iodine. Iodine value = 143·6.
$C_{18}H_{34}O_2$ requires C = 76·6; H = 12·1 per cent. I. V. = 90·1.
$C_{18}H_{32}O_2$ requires C = 77·1; H = 11·4 per cent. I. V. = 181·4.

It would appear from the above results that the liquid acids consisted essentially of a mixture of oleic and linolic acids.

Ether Extract of the Resin.

This extract, on keeping for some time, deposited a quantity of sparingly-soluble material, which was collected by filtration. The filtered ethereal liquid was then extracted successively with aqueous ammonium carbonate, sodium carbonate, and sodium hydroxide. Nothing definite was obtained by this treatment with the exception of a trace of the previously isolated quercetin, which was removed by the sodium carbonate. On finally evaporating the ether only a little fatty matter remained.

The above-mentioned, sparingly soluble material was first extracted in a Soxhlet apparatus with ethyl acetate, and subsequently with alcohol. The ethyl acetate removed a quantity of substance, which was separated into a neutral and an acid portion. The small amount of neutral product was crystallised several times from a mixture of ethyl acetate and alcohol, when it melted constantly at 62-63°, and appeared to be a further quantity of triacontane, $C_{30}H_{62}$ (Found C=85·1; H=14·3; Calc., C=85·3; H = 14·7 per cent.). The acid portion amounted to about 1 gramme. This could only be completely purified from a trace of hydrocarbon by conversion into its ethyl ester, which, when crystallised from a mixture of ethyl acetate and alcohol, melted at 72·5-73·5°, and proved to be ethyl melissate (Found, C = 80·0; H = 13·3. Calc., C = 80·3; H = 13·3 per cent.). On hydrolysis of the ester it yielded melissic acid, melting at 90-91°.

The alcolol extract of the sparingly soloublc material gave the colour reaction of the phytosterols. It was acetylated,

and the product crystallised, when it melted at 164-165°. On regenerating the substance from the acetyl derivative, and crystallising from pyridine, it separated in microscopic needles, melting at 296-297°. After drying at 125-130°, it was analysed.

0·0609 gave 0·1604 CO_2 and 0·0559 H_2O. C = 71·8; H = 10·2.
$C_{33}H_{56}O_6$ requires C = 72·3; H = 10·2 per cent.

It is evident from the characters and composition of this substance that it is a phytosterolin, and apparently identical with that obtained from the petroleum extract of the resin.

Chloroform Extract of the Resin.

This extract, as in the case of the preceding one, deposited a considerable quantity of sparingly soluble material, which was collected. The clear, filtered liquid was then extracted with aqueous alkalis, but these products were small in amount, and nothing definite could be obtained from them.

Isolation of Jambulol, $C_{16}H_8O_4(OH)_5$.

The above-mentioned, sparingly soluble material was gently heated with acetic anhydride, when a small amount of a semi-crystalline substance did not pass into solution and was collected. On subsequently evaporating the acetic anhydride, no further amount of this substance could be obtained from the residue. The semi-crystalline substance was apparently insoluble in all the usual solvents with the exception of pyridine, from which, after several crystallisations, it was collected in four fractions. The first two of these consisted of long needles, having a greyish lustre, but on keeping they gradually lost pyridine of crystallisation and became dull-brown in colour. They did not melt at a temperature of 375°. As the third fraction did not appear perfectly homogeneous, it was again heated with acetic anhydride, and the product crystallised from nitrobenzene, when it separated in microscopic, grey needles, melting and decomposing at 335-340°. The fourth fraction, although similar in appearance to the first two fractions, melted at 335-340°, and on further treatment with acetic anhydride this melting point remained unchanged. It was then crystallised from nitrobenzene, and found to be identical with the product from the third fraction.

In order to ascertain whether the fractions of substance which did not melt at 375° consisted to any extent of acetylated produots, the second fraction was heated with an alcoholic solution of potassium hydroxide, but it was completely decomposed by this treatment. From the characters of the fractionated products above described, it seemed probable that the semi-crystalline substance consisted of jambulol, of which only a part had become acetylated by the treatment of the original crude material with acetic anhydride. A known specimen of jambulol was therefore subjected to the action of

caustic alkali, when, as in the case of the above-mentioned substance, it was found to become decomposed.

A small portion of the first fraction was subsequently benzoylated, and the product crystallised from pyridine, when it separated in small colourless needles, which softened at 328° and melted at 331°. Another portion of the same fraction was first boiled with alcohol to remove traces of pyridine, then dried at 130° and analysed.

0·0544 gave 0·1114 CO_2 and 0·0117 H_2O. C = 55·8; H = 2·4.
$C_{16}H_8O_4(OH)_5$ requires C = 55·8; H = 2·3 per cent.

The identity of the above-described substance as jambulol was thus completely established. This compound, which had been found in considerable amount in jambul seed[5] (from *Eugenia Jambolana*, Lam.), and was then completely characterised, has also been observed to occur in very minute quantity in Chinese rhubarb.[6] In the present instance the total amount isolated from 20·07 kilogrammes of the *Euphorbia* herb was about 0·25 gramme.

Ethyl Acetate and Alcohol Extracts of the Resin.

These two extracts were dark in colour, and entirely amorphous. They were separately heated with dilute sulphuric acid in aqueous alcohol, and the mixture subsequently distilled in a current of steam. The distillates, when extracted with ether, yielded in each case a trace of oily liquid, which gave the colour reaction of furfuraldehyde. The aqueous, acid liquids, on extraction with ether, yielded a trace of crystalline substance, which appeared to be identical with the previously described compound, $C_{28}H_{18}O_{15}$. From the liquid resulting from the above treatment of the alcohol resin a small amount of an osazone (m.p. 196-199°) was prepared, thus indicating the presence in this resin of a little glucosidic material.

Summary.

The material employed for the present investigation of *Euphorbia pilulifera*, Linné (Nat. Ord. *Euphorbiaceæ*), consisted of the entire plant, which had been specially collected for the purpose in the Fiji islands.

The air-dried material (20·07 kilogrammes), when extracted with hot alcohol, and the resulting extract distilled in a current of steam, yielded a small amount (3·7 grammes) of a pale yellow essential oil.

From the portion of the alcoholic extract which was soluble in water, the following substances were isolated :—(i.) Gallic acid; (ii.) quercetin, $C_{15}H_{10}O_7$; (iii.) *a new phenolic substance*, $C_{28}H_{18}O_{15}$. The aqueous liquid contained, furthermore, a considerable quantity of amorphous glucosidic material, together with a lævorotatory sugar which yielded

[5] *Pharmaceutical Journal*, 1912. **88**, 416.
[6] *Journ. Chem. Soc.*, 1911, **99**, 962.

d-phenylglucosazone (m.p. 218-220°). There were also indications of the presence of an exceedingly small amount of alkaloidal substance, but this did not permit of being further characterised.

The portion of the alcoholic extract which was insoluble in water consisted of soft, resinous material, amounting to about 3·2 per cent. of the weight of the air-dried plant. From this material there were isolated : (i.) Triacontane, $C_{30}H_{62}$, with apparently a little ceryl alcohol, $C_{27}H_{56}O$; (ii.) a new monohydric alcohol, *euphosterol*, $C_{25}H_{39}\cdot OH$ (m.p. 274-275°), which yielded an *acetyl* derivative (m.p. 295-297°) and a *bromoacetyl* derivative (m.p. 183-186°). Euphosterol is evidently closely related to the compounds designated respectively as androsterol, homoandrosterol (*Journ. Chem. Soc.*, 1909, **95**, 739), taraxasterol, and homotaraxasterol (*Ibid.*, 1912, **101**, 2,425), all of which appear to be members of a series of monohydric alcohols represented by the general formula, $C_nH_{2n-10}O$. (iii.) A phytosterol (m.p. 132-133°); (iv.) a phytosterolin (phytosterol glucoside); (v.) jambulol, $C_{16}H_3O_4(OH)_5$; (vi.) melissic acid, $C_{30}H_{60}O_2$, and a mixture of acids which appeared to consist chiefly of palmitic, oleic, and linolic acids.

Among the various above-mentioned constituents of *Euphorbia pilulifera* there is none to which any specific physiological action may be ascribed. Such therapeutic virtues as the plant has been presumed to possess would therefore not appear to depend upon any single substance of a definite chemical character.

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